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10/542,495	01/18/2006	Etienne-Emile Baulieu	03715.0148	7023

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EXAMINER	
CHUI, MEI PING	

ART UNIT	PAPER NUMBER
1616	

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01/25/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,495	BAULIEU ET AL.	
	Examiner	Art Unit	
	MEI-PING CHUI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/01/2010 & 11/04/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,11,12 and 14-31* is/are pending in the application.

4a) Of the above claim(s) *7,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8 and 14-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 July 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Receipt of Amendments/Remarks filed on 11/04/2010 is acknowledged. Claims 1-8, 11-12 and 14-31 are pending in this application. Claims 9-10 and 13 have been cancelled; claims 1-2 and 8 have been amended; new claims 14-31 are added.

Upon further consideration, the Examiner has withdrawn the previous election of species requirement for the treated disease in view of the discussion at the interview (see: Interview Summary PTO-413 dated on 06/08/2010).

Applicants' claim amendments necessitated the new grounds of rejection presented in this office action. Accordingly, this action is made final.

Priority

Acknowledgment is made of Applicants' claim for foreign priority based on an application filed in France on 01/17/2003. However, it is noted that Applicants have not filed a certified copy of the English translation of the foreign application No. 03/00507 as required by 35 U.S.C. 119(b).

Status of Claims

Accordingly, claims 1-6, 8 and 14-31 are presented for examination on the merits for patentability as they read upon the elected subject matter and claims 7 and 11-12 directed to non-elected invention are withdrawn.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejection(s) is/are either reiterated or newly applied.

They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Response to arguments

Applicants arguments filed on 11/04/2010 have been fully considered and they are mooted in view of the new grounds of rejection necessitated by the claim amendments and the new claims.

New Ground of Objection/Rejection

The drawing disclosure is objected to because of the following informalities: The legend of "Figure n°4" should be corrected to "Figure 4". Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement of the Invention

Claims 1-6, 8 and 14-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Firstly, claims 14 and 28 while being enabling for the compounds: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG); 3β-methoxy-pregna-5-ene-20-one-17α-dichloromethyl and 3β-methoxy-5α-pregnane-20-one, the claims do not reasonably provide enablement for the other compounds: 3β-methoxy-pregna-5,14-diene-20-one; 3β-methoxy-PREG-16α,17α-epoxy and 3β-methoxy-PREG-16α,17α-methylene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

Secondly, claims 1, 14, 19, 24 and 28 while being enabling for treating medullary trauma, the claims do not reasonably provide enablement for the treatment of other diseases, namely Parkinson's disease, aged-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of spinal cord, pain, notably neuritic pain, nerve degeneration (Alzheimer's disease), and multiple sclerosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

An analysis of whether the scope of a particular claim is actually supported by the disclosure in a patent application requires a determination of whether the disclosure, at the time of filing, contained sufficient information regarding the subject matter of the claim at issue so as to enable one skilled in the pertained art to use the claimed invention without undue experimentation. In re Wands, 8 USPQ 2d 140 (Fed. Cir. 1988). Therefore, the test of enablement is not whether experimentation is necessary, but rather, if experimentation is in fact necessary, whether it is reasonably considered to be undue.

In re Angstadt, 190 USPQ 214, 219 (CCPA 1976). Determining the issue of enablement with respect to a claim is a question of law based on underlying factual findings. In re Vaeck, 20 USPQ 2d, 1444 (Fed. Cir. 1991). More particularly, there are many factors to be considered in determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, and whether any necessary experimentation is reasonably considered to be "undue". See In re Wands at page 1404. MPEP § 2164.01(a). The court in In re Wands set forth the following factors to be considered, which included, without limitation, the: 1). scope or breadth of the claims; 2). nature of the invention; 3). relative level of skill possessed by one of ordinary skill in the art; 4). state of, or the amount of knowledge in, the prior art; 5). level or degree of predictability, or a lack thereof, in the art; 6). amount of guidance or direction provided by the inventor; 7). presence or absence of working examples; and 8). quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Scope or breadth of the claim:

(1) Claims 14 and 28 are broader in scope than the enabling disclosure. The specification merely, without more, discloses the compounds: 3β-methoxy-pregna-5,14-diene-20-one; 3β-methoxy-PREG-16α,17α-epoxy and 3β-methoxy-PREG-16α,17α-methylene are effective to stimulate the polymerization of microtubules induced by MAP2 and to stimulate neuritic sprouting. However, Applicants are claiming all of these

claimed compounds can effectively treat an acute or chronic spinal cord lesion, or Alzheimer's disease, even though the results obtained from the stimulation of neuritic sprouting experiment showed that the compounds PREG-16α,17α-epoxy and PREG-16α,17α-methylene (which are the parent compounds of 3β-methoxy-PREG-16α,17α-epoxy and 3β-methoxy-PREG-16α,17α-methylene), as well as 3β-methoxy-pregna-5,14-diene-20-one produced lower neuritic sprouting stimulation than that produced by the control (pregnenolone) (see Specification: page 21-22, Example 10).

(2) Claims 1, 14, 19, 24 and 28 are also broader in scope than the enabling disclosure for the diseases that can be effectively treated by the claimed compounds, i.e. 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG or named as 43B in the examples). Although the specification showed the speed of motor function recovery from the claimed compound 3-methoxy-PREG (or named as 43B) is faster compared to the control (pregnenolone) (see Specification, page 18, Example 5 and Figure 7); however, there is no experimental data and evidence to further support the claimed compounds can treat spinal cord lesion and Alzheimer's disease.

Nature of the invention:

The nature of the invention is directed to methods of treating an acute or chronic spinal cord lesion (e.g. medullary compression) or Alzheimer's disease by administering to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG) and its analogues therein.

Amount of guidance or direction provided by the inventor, and presence or absence of working examples:

The specification provides few results and working embodiments with respect to the administration of the compound: 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG or compound 43B) for treating medullary trauma and the stimulation of neuritic sprouting. However, in the specification, there is no working example(s) to show the effectiveness of other claimed compounds for treating the claimed diseases, namely acute or chronic spinal cord lesion, and Alzheimer's disease. Although the specification provides an example of in vivo experiments for Alzheimer's-type neurodegenerative disease model using the compound 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG or as compound 43B in the specification), the specification does not clearly explain how the graphical results disclosed in the specification correlates to the treatments as claimed, especially when the graphical result does not correspond to the description in the specification (see Specification, page 19, Example 7 and Figure 8).

Level or degree of predictability, or a lack thereof, in the art:

A high degree of unpredictability exists in the state of the art regarding how to treat Alzheimer's disease and spinal cord lesion. At this stage of the art, the causes and mechanism of these diseases such as Alzheimer's disease, are still unknown and the factors that may trigger these diseases still cannot be controlled, such as the factors due to the potential genetic one inherits from their parents, or other unknown promoting factors.

In particular, there are still a great deal of uncertainty and limitation of current treatments and approaches existed in the state of the prior art regarding the aspects of bioavailability, dose-related symptoms and adverse effects that all may limit the ability to titrate drugs up to efficacious doses. Since such limitations existed in the relevant

research field related to the instant invention that requiring each embodiment of the invention to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue.

Further, their mode of action is often unknown or very unpredictable and administration of the claimed compounds can be accompanied by undesirable side effects such as additive or antagonistic effect as opposed to synergism. Thus, in the absence of a showing of correlation between all the compounds as claimed, and their ability to stimulate the polymerization of microtubules and neuritic sprouting, one of ordinary skill in the art is unable to fully predict possible results from the administration of all of the claimed compounds, due to the unpredictability of the causes of Alzheimer's disease and chronic spinal lesion, can be encompassed in the manner as claimed.

The quantity of experimentation needed is undue because one of ordinary skill in the art would first need to determine, for example, the types of spinal cord lesion to be treated, and then determine which claimed compounds would be effective for the treatment of those types of lesions, with no assurance of success.

Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure:

One of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the claimed compounds and corresponding method of the instant application does in fact effectively treat the

claimed acute or chronic spinal cord lesion, or Alzheimer's disease in the instant invention.

In conclusion, it is readily apparent from the aforementioned disclosure, in conjunction with a corresponding lack of scientific data and working embodiments regarding the claimed compounds and the formula (I) and the claimed diseases: an acute or chronic spinal cord lesion, or Alzheimer's disease, claims 1-6, 8 and 14-31 are not enabled because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

For these reasons, Applicants are required to provide additional guidance and direction with respect to how to use the claimed subject matter in claims 1-6, 8 and 14-31 in order for the application to be to the full scope of the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 has been amended to recite "according to claim 1, the acute or chronic spinal cord lesion is medullary compression". The claim is indefinite because the term "spinal cord lesion" is related to the spinal cord of the body; however, "medullary

compression" is related to medulla of the body, which is also a part of the brain. Since the brain is not equivalent to the spinal cord of the body, it is unclear what Applicants intend to claim with respect to the disease treatment recited in claim 2.

In addition, the term "medullary compression" is indefinite because this term "medullary compression" cannot be found in the existing information available in the relevant art.

Claim Rejection - 35 U.S.C. § 102

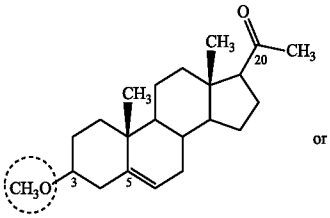
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102(a) that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless:

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

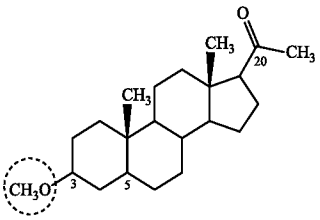
Claims 19-31 are rejected under 35 U.S.C. 102(a) as being anticipated by Baulieu et al. (EP 1310258).

Instant claims are drawn to a method of treating Alzheimer's disease in a patient comprising administering to a patient of a composition, which comprises 3β-methoxy-pregna-5-ene-20-one (3-methoxy-PREG: represented by the structure as follows) or the formula I (represented by the structure as follows) derived from pregnenolone that contains a 3-methoxy function:



3β-methoxy-pregne-5-ene-20-one

or



the formula I (i.e. 3β-methoxy-5α-pregnane-20-one) ;

wherein the composition is administered by injection or orally.

The prior art Baulieu et al. disclose a method for the enhancement of memory and cognitive functions by administering tot he individual a therapeutically effect amount of an enantiomer of a steroid, wherein the individual has suffered memory loss resulting from a cause of neurodegenerative disorders, i.e. Alzheimer's disease (page 3: [0010-0014, 0016]; page 5: [0027]).

Baulieu et al. also disclose that the suitable steroid enantiomer, i.e. 3β-methoxy-pregna-5-ene-20-one or 3β-methoxy-pregnane-20-one, can be used (page 4: [0017], line 7, 14), and wherein the typical administered dosage of the steroid enantiomer fall within the range of from about 0.1 to about 5 mg/kg of a patient's weight, or preferably about 1 mg/kg of a patient's weight (page 5: [0032]). It is noted that the dosage discloses by Baulieu et al. can be calculated corresponding to 7-350 mg or, preferably, 70 mg per an average 70 kg body weight.

Baulieu et al. further disclose that the composition also comprises a pharmaceutically acceptable carrier or excipient, and the composition can be administered by parenterally, i.e. injection, or orally (page 5: [0030], line 1-6, 10; page 6: column 9, line 3, Example 3 for treatment and injection procedure).

With respect to the limitation where the composition is administered to the patient in an amount effective to stimulate polymerization and/or stabilization of microtubules in

the patient, it is noted that Baulieu et al. disclose the steroid 3β-methoxy-pregna-5-ene-20-one and 3β-methoxy-pregnane-20-one, which are identical to the compounds as claimed. Since a chemical compound and its properties are inseparable. Therefore, if the prior art discloses the identical chemical structure, the properties applicant discloses and/or claims are necessarily present (see MPEP 2112.01: Part II and also see In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Response to Arguments

Applicants' argument filed on 11/04/2010 have been fully considered, but they are not persuasive.

Applicants argue that Baulieu is not prior art under 35 U.S.C. § 102(a). Baulieu was published on May 14, 2003, while Applicant's French priority application was filed on January 17, 2003. Thus, Applicant's effective filing date antedates the publication date of Baulieu. Applicant draws the Examiner's attention to the fact that EP 1 310 258 is the priority application of PCT application WO 03/039554, which was filed in the English language on November 8, 2002, and published on May 15, 2003, but this PCT application does not seem to have entered U.S. (see Remarks: page 20).

The arguments are not persuasive because the invention was described in a printed publication in a foreign country by the prior art Baulieu et al. (EP 1310258 published on 05/14/2003) before the invention was originally filed. Although Applicants claim for priority application of PCT/FR04/00086 on 01/16/2004 (which is filed and published in French), which claims the benefit of an earlier filing date based on a foreign application (FR 03/00507) filed in France on 01/17/2003, Applicants have not filed a

certified copy of the English translation of the foreign application FR 03/00507 as required by 35 U.S.C. 119(b). Therefore, Applicants' effective filing date does not antedate the publication date of Baulieu et al. As such, Baulieu et al. (EP 1 310 258) which is filed and published before the priority application of PCT/FR04/00086 is a proper prior art available under 35 U.S.C. 102(a).

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new grounds of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b) and § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either PRIVATE PAIR or PUBLIC PAIR. Status information for unpublished applications is available through PRIVATE PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the PRIVATE PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/H. C./

Examiner, Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616